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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,491	06/09/2006	Michiyo Yanase	YAMAP0997US	9721

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	PAPER NUMBER
1652	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,491	YANASE ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 January 1940*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *20-33 and 35-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/12/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-40 are present in this application.

2. **Election**

Applicant's election of Group I (claims 1-19 & 34; SEQ ID NO: 2 & motif sequence 3L (or SEQ ID NO: 47) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. **Claims withdrawn** :

Claims 20-33 & 35-40 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. ***Priority***

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers [JP 2003-173972] submitted under 35 U.S.C. 119(a)-(d), which papers [certified copy] have been placed of record in the file.

5. ***Drawings***

Drawings filed on 12/12/2005 is acknowledged.

6. ***Sequence Rules***

The instant specification in drawing - **Figures 1A-1I** and through-out the **specification** and **claims**, present amino acid sequences (motif sequences – SEQ ID NO: 45-48); that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but fails to comply with the requirements. According to 37 CFR 1.821-825, every disclosed amino acid sequence of **four or more** residues or 10 or more nucleotides must be identified by a SEQ ID NO. The amino acid sequences presented do not have SEQ ID Nos. In order to comply with the sequence rules Applicants must identify these sequences by providing SEQ ID NO:, and where required provide a new version of the sequence listing and disk.

Applicant must submit a CRF copy and paper copy of the Sequence Listing, a statement that the content of the paper and computer readable copies are the same and where applicable include no new matter as required by 37 C.F.R. j 1.821(e) or 1.821(9

or 1.821(g) or 1 .825(d), as well as an amendment directing its entry into the specification.

Note: The motif sequences have designated SEQ ID Nos., which may be used to amend the specification and claims accordingly.

However, it is not clear if Figure 1A-1I presenting sequence comparisons have the required SEQ ID Nos. in the present sequence listing. If the sequence identifier numbers are present – the figure legend may be amended to indicated the necessary changes.

Specification

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

8. ***Claim Objections***

Claims 1-19 and 34 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims are objected for reciting non-elected subject matter. Applicants are required to cancel the non-elected subject matter in response to this Office Action.

9. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Enablement Rejection

Claims 3-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated α-glucan phosphorylase having improved thermo stability, which is obtained by modifying a natural α-glucan phosphorylase, wherein the natural α-glucan phosphorylase is obtained from a plant, and the α-glucan phosphorylase having improved thermo stability has an amino acid residue which is different from that of the natural α-glucan phosphorylase in a position corresponding to position 7 in a motif sequence 3L: R-I-V-K-F-I-T-D-V of SEQ ID NO: 47; and wherein enzyme activity of the α-glucan phosphorylase having improved thermo

stability at 37°C, after heating in a 20 mM citrate buffer (pH 6.7) at 60°C for 10 minutes, is 20% or more of enzyme activity of the α-glucan phosphorylase having improved thermo stability at 37°C, before heating; does not reasonably provide enablement for the natural α-glucan phosphorylase (SEQ ID NO: 2) to having *varying sequence homology* of 50% with respect to the to the sequences of SEQ ID NO: 2. or wherein the natural α-glucan phosphorylase of SEQ ID NO: 2 be hybridized under stringent conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO: 2. Other α-glucan phosphorylase sequences being disclosed in the specification.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of protein of SEQ ID NO: 2 by 50%, because the

specification does **not** establish: (A) regions of the protein structure which may be modified without effecting α-glucan phosphorylase activity; (B) the general tolerance of α-glucan phosphorylase enzyme to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any α-glucan phosphorylase enzyme residues with an expectation of obtaining the desired enzymatic or biological function and being thermostable and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

With regard to claims 4, wherein the natural α-glucan phosphorylase encoded by nucleic acid sequence that hybridizes to the disclosed sequences, Applicants have not sufficiently defined the conditions under which the hybridizations are to take place. Nucleic acid hybridization assays are extremely sensitive to the conditions in which they are performed. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid, are all variables which determine the reproducibility of a given hybridization experiment. Given the unpredictability of the art and the nature of hybridization experiments in general, it is not sufficient to merely cite hybridization without a clear and explicit recitation of the conditions associated with the hybridization. For example, the definition of stringency as it pertains to hybridization conditions is subject to interpretation and is different from laboratory to laboratory. Therefore, without a clear and explicit recitation of the conditions which were actually used by Applicants in isolating the claimed polynucleotides which hybridize to the disclosed sequences, the skilled artisan would not be able to practice the claimed invention and would not be reasonably apprised of the metes and bounds of the claimed invention. Without such guidance, the experimentation left to those skilled in the art is undue. Including in the claims the exact nature of the hybridization *high stringent* conditions used to isolate the claimed polynucleotides would aid in overcoming this portion of the rejection.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

Without sufficient guidance, determination of exact nature of the α-glucan phosphorylase enzyme and the variants thereof is unpredictable and the experimentation left to those skilled in the art is improper, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

10. Claims 3-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses the reduction to practice of one elected species and several non-elected species within the claimed genus; specifically, the protein having the amino acid sequence of SEQ ID NO: 2. There are no drawings or structural formulas disclosed of any other protein having the function of α-glucan phosphorylase enzyme, other than the sequence homology comparison in Figure 1 (A-I). There is no teaching in the specification regarding the 50% structure that can be varied while retaining the ability of the protein to function as a α-glucan phosphorylase enzyme and be thermostable. Further, there is no art recognized correlation between any structure (other than SEQ ID NO: 2) and the α-glucan phosphorylase enzyme activity. Consequently there is no information about which amino acids can vary from SEQ ID NO: 2 in the claimed genus and still retain the catalytic activity.

Although the disclosure of SEQ ID NO: 2 combined with the knowledge would put one in possession of proteins that are at least 50% identical to SEQ ID NO: 2, the level of skill and knowledge in the art is such that one of ordinary skill would not be able to identify without further testing which of those proteins having at least 50% identity to SEQ ID NO: 2 (if any) and having the activity of α-glucan phosphorylase enzyme. Based on the lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that Applicant was in possession of the claimed genus of proteins based on the disclosure of several naturally occurring proteins having α-glucan phosphorylase enzyme activities without guidance to specific modifications.

11. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 1-19 & 34 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 & 34 recite the phrase(s) – 'derived from a plant' or 'Plant-derived', which phrase(s) are vague in the context used. Substituting the phrase(s) with - 'obtained from a plant' is suggested to overcome this rejection.

Claims 2-19 are included in the rejection for failing to correct the defect present in the base claim(s).

12. **35 U.S.C. § 101**

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-19 & 34 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims 1 & 24 to recite wording such as "An isolated α-glucan phosphorylase ".

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on (571) 272 0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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